

REMARKS

The Examiner is thanked for the thorough examination of the application. The specification has been amended to improve the language.

Claims 1, 2 and 4-18 are pending in the application. Acknowledgement of the allowability of claim 7 is noted with appreciation. Allowable claim 7 has been amended to stand as an independent claim, thus obviating the objections to that claim.

Rejection Under 35 USC §103(a)

Claims 1, 2, 4-6 and 8-18 have been rejected under 35 USC §103(a) as being unpatentable over SCHNEIDER et al. (Journal of Vascular Surgery). This rejection is respectfully traversed for at least the reasons set forth below.

The present invention pertains to an intraluminal device with a coating to improve vascular healing and to prevent thrombosis. The coating mainly includes a constituent with an anti-thrombogenic effect to minimize thrombosis. Additionally, in order to improve vascular healing, the coating includes constituents that improve binding of endothelial cells to the coating and constituents that contribute to the binding properties of the coating. Further, the coating includes constituents that improve attachment of the coating to the intraluminal device. For optimal characteristics, the inventors have carefully tailored the coating to contain these constituents in specific amounts.

Independent claims 1 and 12 of the present invention thus recite a coating that includes 50-97% heparan sulfate, 1-20% laminin and 0.2-15% type IV collagen.

SCHNEIDER et al. describe coating of vascular graft material with subendothelial extracellular matrix (ECM) naturally produced by endothelial cells (ECs). The ECM is found to include a broad range of different proteins, and primarily contains collagens of type I, III, IV and V, heparan sulfate-proteoglycans, dermatan sulfate-proteoglycans, laminin, nidogen, fibronectin, and elastin.

However, there is no disclosure whatsoever in SCHNEIDER et al. that the constituents of the present invention are present in the coating at the specific claimed concentrations.

More specifically, SCHNEIDER et al. fail to disclose the use of heparan sulphate (50% or greater) as a major component in the coating in order to prevent thrombosis. Therefore independent claims 1 and 12 of the present invention are clearly patentable over SCHNEIDER et al.

Furthermore, in view of the natural nature of the related art coatings, it is not obvious for the skilled person to interfere with nature in order to vary the amounts of the constituents in this coating, specifically to reach the amounts according to the present invention.

In fact, on page 655, left column, last paragraph, SCHNEIDER et al. demonstrate the importance of the natural nature

of the coating, because the "naturally produced ECM" supposedly has "superior cell growth-promoting properties" when compared with "isolated constituents of the ECM". Therefore, SCHNEIDER et al. teaches away from using a coating with specifically selected substituents departing from nature.

Moreover, SCHNEIDER et al. is concerned with a coating that improves adhesion and growth of ECs on synthetic graft material. In practice, the bare coating of SCHNEIDER et al. appears to have a proliferative effect with an enhanced probability of thrombosis. Not surprisingly, Schneider teaches to expose the coating to glutaraldehyde or to seed vascular ECs to the coating to create a nonthrombogenic surface to prevent thrombosis. There is no disclosure or suggestion in SCHNEIDER et al. to modify the ECM in an attempt to improve the anti-thrombotic properties.

In the Response to Arguments at page 4, the Official Action asserts:

[O]ptimization of the weight percentages of each is a skill within that of any ordinary practitioner, and for the same art recognized purpose of finding an effective coating for an intraluminal device. As such, the motivation to improve the coating set out by Schneider by modifying the percentages would have been obvious to any ordinary practitioner.

However, the assumption of routine optimization depends on the complexity of the art, and the biochemical/biomedical art of the present invention is both complex and unpredictable.

For example, in *In re Aller*, a straightforward chemical process (the production of phenol and acetone by peroxidation) was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

On the other hand, in *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, a diuretic for oral administration included combinations of amiloride hydrochloride and hydrochlorothiazide. The Circuit Court found that the applied prior art did not describe or forecast the effects that the combined drug would have on such factors as sodium excretion, potassium excretion and ratio of sodium excretion to potassium excretion. "A composition must be assessed for obviousness only after consideration of its chemical structure as well as its pharmaceutical and biological properties." *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989).

The present invention, similar to *Merck*, combines components in specific amounts to achieve a synergistic therapeutic effect, in this case of maintaining the binding characteristics of the coating while preventing thrombosis. This

unexpected result is clear from the Example of stents implanted in swine at page 7 of the specification.

As a result, one of ordinary skill in the art would not be motivated by SCHNEIDER et al. to produce independent claims 1 and 12 of the present invention. A *prima facie* case of unpatentability has not been made. Claims depending upon independent claim 1 or 12 are patentable for at least the above reasons. This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Allowable Subject Matter

The Examiner is thanked for indicating the allowability of claim 7. Claim 7 has been amended to stand as an independent claim and is thus instantly allowable.

Conclusion

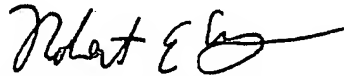
The Examiner's rejection has been overcome, obviated or rendered moot. No issues remain. The Examiner is accordingly respectfully requested to place the application in condition for allowance and to issue a Notice of Allowability.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 25-0120 for any additional
fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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